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Diagnostic Value Of Serum Adenosine Deaminase In Type 2 Diabetes Mellitus

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Abstract
BACKGROUND - Adenosine deaminase (ADA) is suggested to modulate the bioactivity of insulin. The present study was undertaken to evaluate serum ADA activity and serum uric acid levels in patients of Type 2 DM.
AIM: To evaluate the serum ADA level and to correlate ADA levels with Blood Glucose, Glycated Hemoglobin (HbA1c) levels in Type-2 DM patients.
MATERIAL AND METHOD: It is a case control study. The subjects in this study were divided into 3 groups. Group I consisted of 50 normal healthy individuals who served as controls with no history of DM. Group II consisted of 50 patients of Type 2 DM both males & females in the age group of 40-65 years on oral hypoglycemic drugs with HbA1c <7%. Group III consisted of 50 patients of Type 2 DM both males & females in the age group of 40-65 years on oral hypoglycemic drugs with HbA1c >7%. Serum levels of fasting blood sugar, HbA1c, ADA and uric acid were estimated in all the subjects.
RESULTS: FBS, HbA1c, ADA and serum uric acid levels were found to be increased in the patients of Type 2 DM as compared with controls.
CONCLUSION: It is concluded that there is an increase in serum ADA levels with increase in HbA1c levels. Serum uric acid levels increased with moderately increasing levels of HbA1c >7% and then decreased with further increasing levels of HbA1c >7% (a bell-shaped relation).
Keywords : *Type 2 diabetes mellitus , Serum ADA , HbA1c , serum uric acid.*

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I. INTRODUCTION

Diabetes Mellitus is one of the most important factors of mortality in the developing countries and it affects more than 170 million people all over the world. Type 2 Diabetes Mellitus is characterised by insulin resistance where there is impaired ability of hormone to suppress hepatic glucose output and to promote peripheral glucose uptake and compromised function of pancreatic beta cells such that insulin secretion is insufficient to match the degree of insulin resistance. Adenosine Deaminase, an enzyme catalyses the deamination of adenosine to inosine & 2'-deoxyadenosine to 2'-deoxyinosine. Inosine and 2'-deoxyinosine are converted to hyoxanthine, xanthine and finally uric acid. Adenosine deaminase is considered a good marker of cell mediated immunity. High lymphocyte Adenosine deaminase activities were found in diseases in which there is cell mediated immune response. Adenosine deaminase plays a role in lymphocyte proliferation and differentiation and shows its highest activity in T-lymphocytes. Thus a suppression of Adenosine deaminase activity may help improve various factors associated with the pathophysiology of Type 2 Diabetes Mellitus like insulin sensitivity, inflammation, cell proliferation and T-lymphocyte activity. Adenosine deaminase has been reported to be a marker of insulin function. Adenosine increases glucose uptake inside the cells. Thus higher Adenosine deaminase activity will decrease adenosine levels and thus in turn decreases glucose uptake into cells.

II. MATERIALS AND METHODS

Study Design: Case-control study.

Study Setting: OPD and Medical wards in MAHARAJAH'S INSTITUTE OF MEDICAL SCIENCES , NELLIMARLA and consent was taken from cases and controls before commencing the study.

Sample size: 150 (50controls and 100 cases).

Study Period: DECEMBER 2022 TO AUGUST 2023.

SUBJECT AND SELECTION CRITERIA : A complete clinical examination of subjects was done. About 5ml of fasting blood was collected for the determination of different biochemical parameters. The plasma obtained was analysed for fasting blood sugar (glucose oxidase-peroxidase method), glycated hemoglobin (immunoinhibition method) and serum adenosine deaminase (erba kit).

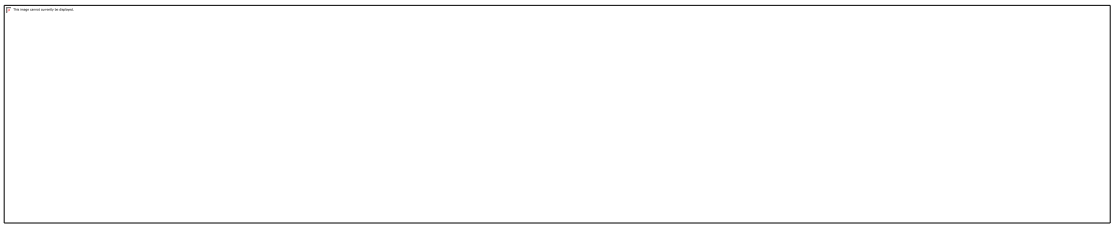
STATISTICAL ANALYSIS : The statistical analysis was performed using students 't' test to compare mean values of variables in control and different groups of diabetes mellitus. The correlations were assessed by Pearson rank correlation coefficient. Differences were considered statistically significant when $p<0.001$.

INCLUSION CRITERIA : The study population comprised of 50 normal healthy individuals both males and females in the age group of 40-65 years as controls in GROUP 1. 50 patients of Type 2 Diabetes Mellitus both males and females in the age group of 40-65 years with HbA1C<7% in GROUP 2. 50 patients of Type 2 Diabetes Mellitus both males and females in the age group of 40-65 years with HbA1C>7% in GROUP 3.

EXCLUSION CRITERIA : Type 1 Diabetes Mellitus ,Tuberculosis, Gout, Rheumatoid arthritis, Skeletal muscle injury, Gross Congestive cardiac failure, Renal failure, Patients on glucocorticoids, thyroid hormones, thiazides, diazoxides, phenytoin, interferons, Patients with history suggestive of any infections at the time of study, Immunological disorders, Trauma or malignancy.

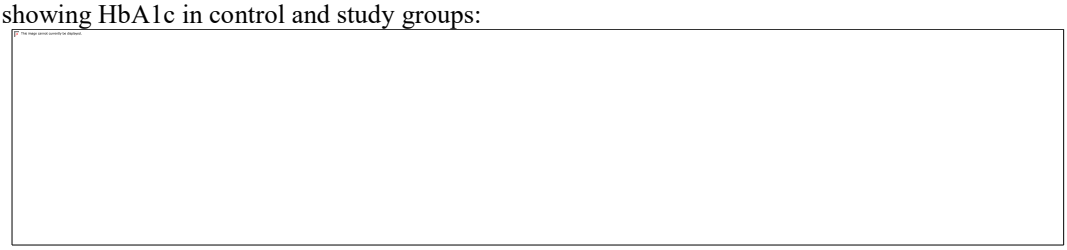
III. RESULTS

Table showing Fasting blood glucose in control and study groups:



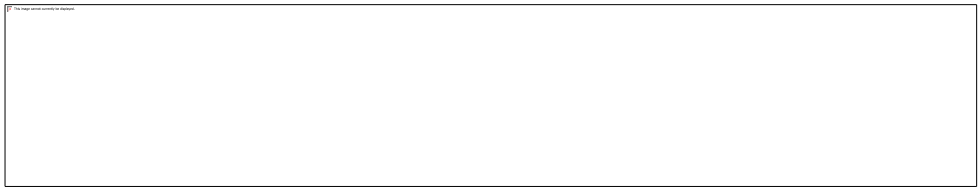
In the present study, the mean FBS levels of Group 2 and Group 3 were found to be significantly higher than Group1($p<0.001$). Although the mean FBS levels of Group 3 were higher than Group 2 but the difference was statistically not significant($p=0.114$).

Table showing HbA1c in control and study groups:



- From this study it was observed that the difference in levels of HbA1c was found to be insignificant between Group1 and Group 2 ($p=0.310$).
- Statistical analysis showed that the mean serum ADA values of Group 3 were significantly higher than Group2($p<0.001$) and the levels of ADA were significantly higher in both Group 2 and Group 3 as compared to Group1($p<0.001$).

- COMPARISION OF SERUM ADA AND HbA1C IN GROUP 2 AND GROUP 3:



- In Group2,the Pearson's correlation coefficient for the relationships between ADA and HbA1c showed positive correlation(r=0.003).
- In Group3,there was positive correlation between ADA and HbA1c(r=0.122).

IV. DISCUSSION

- In the present study,the mean serum ADA levels of Group 3 were significantly higher than Group 2($p<0.001$).Also the levels of ADA were significantly higher in both Groups 2 and 3 than Group 1($p<0.001$).
- Adenosine is both a metabolic precursor for nucleic acids and a signalling molecule involved in various physiological processes. It mimics the action of insulin on glucose and lipid metabolism in the adipose tissue and myocardium. It also potentiates insulin action in skeletal muscle by upregulating GLUT-4.
- A1 receptors of adenosine have been found to be associated with increased insulin sensitivity.
- Adenosine deaminase inactivates adenosine and enhances lipolysis. Thus depletion of adenosine due to increased ADA activity would mean increase in insulin resistance.
- Hyperglycemia leads to activation of NADPH oxidase forming free radicals, thereby causing oxidative stress which in turn increases insulin resistance. It also causes formation of Advanced Glycation End Products(AGEs) as a result of reactions between intracellular glucose derived dicarbonyl precursors with the amino groups of intra and extra-cellular proteins.
- AGEs stimulate receptors for advanced glycation end products(RAGE). Advanced glycation end products bind to AGE receptors on several cell types(endothelial cells,macrophages) and lead to release of cytokines:TNF-α,IL-1,IL-6 and growth factors from macrophages and mesangial cells resulting in proliferation and activation of T-lymphocytes.
- High Adenosine deaminase activity is present in T-cells and due to abnormal proliferation as occurs in hyperglycemia, the Adenosine deaminase in T-lymphocytes spill into circulation.
- The positive correlation between serum ADA and HbA1c in Group 2 & Group 3 shows that with the increase in glycated hemoglobin levels, levels of serum ADA also increases.

V. CONCLUSION

In the present study, significantly higher values of Adenosine deaminase in cases compared to controls suggest that Adenosine deaminase plays a role in the pathophysiology of Diabetes Mellitus and its complications. A positive correlation between Adenosine deaminase level with good and poor glycemic control suggests its role in modulating the bioactivity of insulin. Thus increased activity might be a marker for insulin resistance. Therefore estimation of serum Adenosine deaminase might also serve as a glycemic marker for assessing the glycemic status of a diabetic individual. Larger and more elaborated studies are required at molecular level to know the role of Adenosine deaminase in the pathogenesis of Type 2 Diabetes Mellitus and its complications.

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